Costeff syndrome

Costeff syndrome is a condition characterized by vision loss, movement problems, and intellectual disability. People with Costeff syndrome have degeneration (atrophy) of the optic nerves, which carry information from the eyes to the brain. This optic nerve atrophy often begins in infancy or early childhood and results in vision loss that worsens over time. Some affected individuals have rapid and involuntary eye movements (nystagmus) or eyes that do not look in the same direction (strabismus).

Movement problems in people with Costeff syndrome develop in late childhood and include muscle stiffness (spasticity), impaired muscle coordination (ataxia), and involuntary jerking movements (choreiform movements). As a result of these movement difficulties, individuals with Costeff syndrome may require wheelchair assistance.

While some people with Costeff syndrome have intellectual disability that ranges from mild to moderate, many people with this condition have normal intelligence.

Costeff syndrome is associated with increased levels of a substance called 3-methylglutaconic acid in the urine. The amount of the acid does not appear to influence the signs and symptoms of the condition. Costeff syndrome is one of a group of metabolic disorders that can be diagnosed by the presence of increased levels of 3-methylglutaconic acid in urine (3-methylglutaconic aciduria). People with Costeff syndrome also have high urine levels of another acid called 3-methylglutaric acid.

Frequency

Costeff syndrome affects an estimated 1 in 10,000 individuals in the Iraqi Jewish population, in which at least 40 cases have been described. Outside this population, only a few affected individuals have been identified.

Genetic Changes

Mutations in the *OPA3* gene cause Costeff syndrome. The *OPA3* gene provides instructions for making a protein whose exact function is unknown. The OPA3 protein is found in structures called mitochondria, which are the energy-producing centers of cells. Researchers speculate that the OPA3 protein is involved in regulating the shape of mitochondria.

OPA3 gene mutations that result in Costeff syndrome lead to a loss of OPA3 protein function. Cells without any functional OPA3 protein have abnormally shaped mitochondria. These cells likely have reduced energy production and die sooner than normal, decreasing energy availability in the body's tissues. It is unclear why the optic nerves and the parts of the brain that control movement are particularly affected.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 3-methylglutaconic aciduria type 3
- 3-methylglutaconic aciduria type III
- autosomal recessive OPA3
- autosomal recessive optic atrophy 3
- Costeff optic atrophy syndrome
- infantile optic atrophy with chorea and spastic paraplegia
- Iraqi Jewish optic atrophy plus
- MGA, type III
- MGA3
- OPA3 defect
- optic atrophy plus syndrome

Diagnosis & Management

These resources address the diagnosis or management of Costeff syndrome:

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/3-methylglutaconic-aciduria
- GeneReview: OPA3-Related 3-Methylglutaconic Aciduria
  https://www.ncbi.nlm.nih.gov/books/NBK1473
- Genetic Testing Registry: 3-Methylglutaconic aciduria type 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0574084/
- MedlinePlus Encyclopedia: Optic Nerve Atrophy
  https://medlineplus.gov/ency/article/001622.htm

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Optic Nerve Atrophy
  https://medlineplus.gov/ency/article/001622.htm
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html
- Health Topic: Optic Nerve Disorders
  https://medlineplus.gov/opticnervedisorders.html

Genetic and Rare Diseases Information Center

- OPA3 defect
  https://rarediseases.info.nih.gov/diseases/5663/opa3-defect

Educational Resources

- American Association for Pediatric Ophthalmology and Strabismus: Optic Nerve Atrophy
  https://aapos.org/terms/conditions/81
- Centers for Disease Control and Prevention: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Centers for Disease Control and Prevention: Vision Loss
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/VisionLossFactSheet.pdf

- Cleveland Clinic: Optic Atrophy
  http://my.clevelandclinic.org/health/articles/optic-atrophy
- Disease InfoSearch: 3-Methylglutaconic Aciduria Type III
  http://www.diseaseinfosearch.org/3-Methylglutaconic+Aciduria+Type+III/34
- Kennedy Krieger Institute: Movement Disorders
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/movement-disorders
- MalaCards: 3-methylglutaconic aciduria, type iii
  http://www.malacards.org/card/3_methylglutaconic_aciduria_type_iii
- Merck Manual Consumer Version: Overview of Optic Nerve Disorders
  http://www.merckmanuals.com/home/eye-disorders/optic-nerve-disorders/overview-of-optic-nerve-disorders
- Orphanet: 3-methylglutaconic aciduria type 3
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=67047
- Scottish Sensory Centre: Optic Atrophy
  http://www.ssc.education.ed.ac.uk/resources/vi&multi/eyeconds/OptAt.html
- University of Michigan Kellogg Eye Center: Optic Atrophy
  http://www.umkelloggeye.org/conditions-treatments/optic-atrophy

Patient Support and Advocacy Resources

- American Foundation for the Blind
  http://www.afb.org/default.aspx
- Jewish Genetic Disease Consortium
  http://www.jewishgeneticdiseases.org/diseases/costeff-optical-atrophy-type-3-methylglutaconic-aciduria/
- Organic Acidemia Association
  http://www.oaanews.org/
- Resource List from the University of Kansas Medical Center: Blind/Visual Impairment
  http://www.kumc.edu/gec/support/visual.html

GeneReviews

- OPA3-Related 3-Methylglutaconic Aciduria
  https://www.ncbi.nlm.nih.gov/books/NBK1473

Genetic Testing Registry

- 3-Methylglutaconic aciduria type 3
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0574084/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28costeff+syndrome%5BTIAB%5D%29+OR+%283-methylglutaconic+aciduria+type+3%5BTIAB%5D%29+OR+%283-methylglutaconic+aciduria+type+iii%5BTIAB%5D%29+OR+%28optic+atrophy+plus+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- 3-METHYLGLUTACONIC ACIDURIA, TYPE III
  http://omim.org/entry/258501

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